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EXAMINER	
COUNTS, GARY W	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,933	DREES ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *14,15,31,32 and 35-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 3/31/04
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Upon further consideration the restriction requirement set forth in the office action filed January 14, 2004, Claims 1-13 and 16 are regrouped with Group II – Claims 17-34. Claims 14 and 15 are withdrawn as non-elected species.

However, the restriction requirement of Group III is maintained. The traversal is on the ground(s) that applicants are not aware of uses for multi-well plates as claimed and that Examiner has not submitted evidence to support its use in methods for determining endotoxins. This is not found persuasive because of reasons of record and further because Ding et al (US 6,645,724) discloses a method in which a microtiter plate comprising an immobilized lipid used for determining endotoxins (col. 11, lines 15-60). Applicant also argues the species requirement and states that the present invention is directed to a method for the assay of lipids and it is not the essence of the present invention to use a particular assay format and that the species are similar enough that it would not create an undue burden for the examiner to examine all species concurrently. This is not found persuasive because the assays are different assays and would require different search strategies and different literature searches. Further, while the searches would be expected to overlap, there is no reason to expect the searches to be coextensive.

The requirement is still deemed proper and is therefore made FINAL.

Note: Since Examiner regrouped Group I with elected Group II and with the election of plate based assays by Applicant; the elected invention thus comprises claims 1-13, 16-30, 33 and 34.

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration believes the named inventor or inventors to be the original and first inventor or inventors of the subject matter which is claimed and for which a patent is sought.

It does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 601.01(a).

It does not state that the person making the oath or declaration has reviewed and understands the contents of the specification, including the claims, as amended by any amendment specifically referred to in the oath or declaration.

Claim Objections

2. Claim 21, and 25-29 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 21 recites "is used for said target lipid in bodily tissue, blood, and serum samples" such use of the kit does not further limit the subject matter of the kit.

Claims 25-29 seem to be directed to a process of using the kit and such process or process steps does not further limit the subject matter of the kit.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. On page 21, paragraph [00069] in the specification. The applicant discloses that a variety of published reports link PI 3-K activity or loss of PTEN activity to cancers and that the inventors expected that PI (3,4,5)P_3 levels are likely to be elevated in cervical, prostate, ovarian, lung and colon cancer. However, applicant has not provided any evidence to support this. The specification does not contain working examples, controls or data to support this. Further, the specification fails to disclose a connection between cancer and assay results of lipids. The applicant does not have possession of the invention as claimed.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a cancer screening method for detection of cancer cells, and detection of the target lipid is an indicator of a cancer cell. The specification on page 6, lines 9-11 discloses that the lipid assay is a cancer screening method for detection of cancer cells, and detection of a predetermined level of the $PI(3,4,5)P_3$ target lipid is an indicator of a cancer cell. On page 21, lines 10-21 the specification discloses that increases in $PI(3,4,5)P_3$ levels occur in cells following growth factor stimulation and that $PI(3,4,5)P_3$ are elevated in some types of cancer. On page 21, paragraph [00069] the specification discloses that a variety of published reports link PI 3-K activity or loss of PTEN activity to cancers. The applicant has not disclosed how one skilled in the art can use the method of detecting lipids to diagnose cancer. Further, the applicant does not establish that the determination of cholesterol, LDL or any other lipoprotein (i.e. lipids) is indicative of a cancer cell. The

specification lacks working examples for cancer detection. Furthermore, it is unclear how the target lipid is an indicator of a cancer cell, as recited in the instant claims (see 112 2nd rejection). Such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to establish if the target lipid is indicative of a cancer cell, one skill in the art would have to know predetermined levels for each different type of target lipid and determine whether an increase or decrease or the presence of the target lipid is indicative of a cancer cell. Further, Applicant has not established that other lipids such as cholesterol are indicative of a cancer cell.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-13, 16-30, 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it lacks a step of exposing receptor to sample suspected of containing target lipid. It is unclear how the method can be performed without this step.

Claim 2, line 11 the recitation "a lipid assay" is vague and indefinite. Is applicant referring to the lipid assay of claim 1 or some other lipid assay. It is recommended to replace "a lipid assay" with --The lipid assay--. See also deficiencies found in claims 2-13, 16, 17-30, 33 and 34.

Claim 2 is vague and indefinite because of the use of an acronym: i.e. PI 3-K. Although the term may have art-recognized meanings, it is unclear if applicant intends to claim the prior art definitions. The term should be defined in the first instance. See also deficiencies of the use of acronyms in claims 4, 7, 9, 22, 26 and 28.

Claim 8 is vague and indefinite because it is unclear how the target lipid is an indicator of a cancer cell. Does an increased level of the target lipid indicate a cancer cell or a decreased level of the target lipid indicate a cancer cell or does the mere presence of the target lipid indicate a cancer cell?

Claim 8 is vague and indefinite because it is unclear what type of cancer cell is being detected.

Claim 13 the recitation "wherein coating step includes" there is insufficient antecedent basis for this limitation. It is recommended to amend claim 13 to depend from claim 12.

Claim 17 is vague and indefinite because it appears that the target lipid is in a sample and it is unclear how a sample can be part of a kit because samples are collected at the time of the assay. See also deficiencies found in claims 24, 26 and 28.

Claim 19 "said multi-well assay plate" there is insufficient antecedent basis for this limitation. It is recommended to amend claim 19 to depend from claim 18.

Claim 20 is vague and indefinite because it is unclear what the function of the primary and secondary antibodies are.

Claim 23 is vague and indefinite because of the use of an acronym: i.e. PH. Although the term may have art-recognized meanings, it is unclear if applicant intends to claim the prior art definitions. The term should be defined in the first instance.

Claim 30, line 3 the recitation "via" is vague and indefinite. It is unclear what the term encompasses.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-7, 9-13, 16-30, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kingsmore et al (US 6,531,283) in view of Czech et al (Us 6,194,173).

Kingsmore et al discloses methods for detecting target analytes of interest. Kingsmore et al disclose that the analyte can be a lipid (col 10, lines 56-65). Kingsmore et al disclose assays in which competitive analogs of the analytes are used. Kingsmore et al disclose that these analogs compete with analytes for specific binding molecules. Kingsmore et al disclose that the analog is a molecule that is similar in structure but different in competition. (col 15, lines 20-36). Kingsmore et al disclose that the analog can be immobilized on solid supports such as microtiter plates (col 18, lines 36-67). Kingsmore et al disclose attachment of the molecules to substrates using avidin-biotin systems. Kingsmore et al disclose that the materials can be packaged together in any suitable combination as a kit for performing the methods (col 22, lines 9-15).

Kingsmore et al differ from the instant invention in failing to specifically teach the target lipid has a stronger affinity to the lipid recognition motif than the competing lipid. Kingsmore et al also fail to specifically teach streptavidin coated microtiter plates.

Czech et al disclose "general receptors for phosphoinositide" or GRPs. Czech et al disclose that these GRPs exhibit high affinity binding to products of the lipid kinase phosphatidylinositol 3-OH (PI(3)Kinase) (col 3). Czech et al disclose that the GRP comprises a structurally and functionally modular protein having a PH domain (col 32).

Czech et al disclose that GST can be fused to the PH region of the GRP. Czech et al disclose that these GRPs have high affinity for polyphosphoinositide. Particularly, PtdIns $(3,4,5)P_3$. Czech et al disclose that GRPs have about two orders of magnitude greater than that of PtdIns$(4,5)P_2$ (analog) (col 68, lines 24-32). Czech et al disclose that the GRPs can be labeled with enzymes and used in ELISA assays (col 37). Czech et al also disclose primary and secondary antibodies used in diagnostic assay (col 48). Czech et al also disclose the immobilization of molecules to streptavidin coated microtitier plates (col 46).

It would have been obvious to one of ordinary skill in the art to incorporate reagents (receptors, anitbodies and analogs) as taught by Czech et al into the method of Kingsmore et al because Kingsmore et al is generic with respect to the lipid to be detected and one would use the appropriate reagent, i.e. GRPs, antibodies and analogs to detect the desired analyte, in this case $PI(3,4,5)P_3$. It would also have been obvious to one or ordinary skill in the art to incorporate streptavidin coated surfaces as taught by Czech et al into the method of Kingsomore et al because Kingsmore et al teaches the use of avidin-biotin systems for immobilization and Czech et al teaches that it is well known in the art to use streptavidin-biotin system. Further, it is well known in the art that streptavidin can be used in place of avidin.

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary W. Counts
Examiner
Art Unit 1641
April 6, 2004